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Application Number

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703-521 1952

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(12) **United States Patent**  
Weiss et al.

(10) Patent No.: **US 6,497,872 B1**  
(45) Date of Patent: **Dec. 24, 2002**

(54) **NEURAL TRANSPLANTATION USING  
PROLIFERATED MULTIPOTENT NEURAL  
STEM CELLS AND THEIR PROGENY**

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(\*) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/486,313**

(22) Filed: **Jun. 7, 1995**

#### Related U.S. Application Data

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application No. 07/726,812, filed on Jul. 8, 1991, now  
abandoned, application No. 08/486,313, which is a contin-  
uation-in-part of application No. 08/385,404, filed on Feb. 7,  
1995, now abandoned, which is a continuation of application  
No. 07/961,813, filed on Oct. 16, 1992, now abandoned,  
which is a continuation-in-part of application No. 07/726,  
812, application No. 08/486,313, which is a continuation-  
in-part of application No. 08/359,945, filed on Dec. 20,  
1994, now abandoned, which is a continuation of application  
No. 08/221,655, filed on Apr. 1, 1994, now abandoned,  
which is a continuation of application No. 07/967,622, filed  
on Oct. 28, 1992, now abandoned, which is a continuation-  
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now abandoned, application No. 08/486,313, which is a  
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Jan. 20, 1995, now abandoned, which is a continuation of  
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abandoned, which is a continuation-in-part of application  
No. 07/726,812, application No. 08/486,313, which is a  
continuation-in-part of application No. 08/149,508, filed on  
Nov. 9, 1993, now abandoned, which is a continuation-in-  
part of application No. 07/726,812, application No. 08/486,  
313, which is a continuation-in-part of application No.  
08/311,099, filed on Sep. 23, 1994, now abandoned, which  
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application No. 08/486,313, which is a continuation-in-part  
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abandoned, which is a continuation-in-part of application  
No. 07/726,812.

(51) Int. Cl.<sup>7</sup> ..... **A01N 63/00; A01N 65/00;  
A61K 48/00**

(52) U.S. Cl. .... **424/93.1; 424/93.2; 424/93.21**

(58) Field of Search ..... **424/93.1, 93.2,  
424/93.21; 514/44**

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#### ABSTRACT

The invention provides methods of transplanting multipot-  
ent neural stem cell progeny to a host by obtaining a  
population of cells derived from mammalian neural tissue  
containing at least one multipotent CNS multipotent neural  
stem cell; culturing the neural stem cell in a culture medium  
containing one or more growth factors which induce multi-  
potent neural stem cell proliferation; inducing proliferation  
of the multipotent neural stem cell to produce neural stem  
cell progeny which includes multipotent neural stem cell  
progeny cells; and transplanting the multipotent neural stem  
cell progeny to the host. Also provided are methods of  
transplanting neural stem cell progeny to a host by obtaining  
an in vitro cell culture containing CNS neural stem cells  
where one or more cells in the culture (i) proliferates in a  
culture medium supplemented with one or more mitogens,  
(ii) retains the capacity for renewed proliferation, and (iii)  
maintains the multipotential capacity, under suitable culture  
conditions, to differentiate into neurons, astrocytes, and  
oligodendrocytes; and transplanting the one or more cells to  
the hose.

32 Claims, 3 Drawing Sheets